and governmental authorities, case studies and the latest publications in value-based assessment (VBA) was performed to summarise the current perception of RWD, and to identify the advantages and challenges of using RWD to support market access and reimbursement. Only 10 guidelines were found from 73 European HTA agencies or governmental authorities which cited RWD as a source for evidence. NICE acknowledges the difficulties of generalising RCT results to clinical practice, and supports the capture and analysis of observational data. In addition, recent developments in VBA anticipate a greater scrutiny of attempts to model natural history in economic evaluations, which may be addressed by using longitudinal observational data. Case studies have shown economic evaluations based on RCT data may lack external validity, and may consequently produce inaccurate estimates of economic endpoints. There is a consensus that RWD are valuable in providing clinical practice evidence on treatment pathways, resource use, long-term natural history and true effectiveness. However, there are methodological challenges (such as lack of randomisation) to be addressed before RWD are widely accepted as a complement to RCTs to support decision-making. RWD are increasingly recognised as a valuable source of evidence for market access and reimbursement, and as a complement to clinical trial evidence. Nevertheless, there are challenges that need to be addressed to ensure real world data provide valid evidence to the decision process.

PHP281

REIMBURSEMENT HURDLES FOR HIGH-COST BRAND-ON-BRAND COMBINATIONS AND IMPACT ON PATIENT ACCESS

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Combinations of high-cost branded drugs are becoming a reality. The synergistic value of combining two potent drugs is expected to considerably bolster the benefit to the patient in terms of efficacy and, in some cases, even safety. However, the synergistic cost of using branded combinations increases exponentially due to longer treatment durations, thus making the total treatment cost unaffordable to European health systems. This poster aims to explore the pricing and reimbursement issues that health systems will encounter during the evaluation of branded combination therapies and potential solutions to make these combinations affordable by the health care systems and ensure patient access to innovative drugs. To meet these objectives, an in-depth review of published sources was conducted, including a thorough analogue assessment. Moreover, targeted interviews with twenty payers involved at different levels of pricing and market access decision-making in the EU5 were also conducted to support analysis. Research revealed that synergistic costs of already expensive monotherapies, further exacerbated by longer duration of treatment, exceed payers' cost thresholds. Therefore, on one hand payers will struggle to award a value-based price for the individual drugs as well as for the combination and will look to discount and/or restrict access. On the other hand, as this approach will not reflect the combination's synergistic value and could threaten the life-cycle indications of each compound, manufacturers may not launch in some markets, thus, limiting patient access. Consequently, it is important to find a balance in setting a value-based price for individual indications and for the combinations to ensure broad patient access. Aligning patient, payer and manufacturer needs is paramount to find a win-win-win solution. In the context of brand-on-brand combinations, traditional pricing models are not the solution and alternative approaches need to be adopted.

PHP282

THE CASE FOR EARLY PAYER ENGAGEMENT

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BACKGROUND: Knowledge of payer evidence requirements is vital to manufacturers who are facing increasing development costs for uncertain market access outcomes. Failure to engage payers early in asset development could result in delay of approval and/or coverage. **OBJECTIVES:** Build the case for early payer engagement as a means of reconciling the needs of payers and manufacturers **METHODS:** A literature search was performed and primary research with key opinion leaders in the US and EU was conducted to characterize 5 early engagement strategies (informal consultation, formal consultation, outcomes-based risk sharing, financial-based risk sharing, and formal partnerships). 7 major markets (Canada, France, Italy, Germany, Spain, UK, and US) were also assessed for their historic use of early engagement models. **RESULTS:** Payers want more manufacturer involvement in evidence development, including input into clinical trial design and RWE development in phases II and III through formal and informal consultations. Articulation of an asset's value story in the peri-launch phase and negotiations with regional and local payers through direct consultations allows manufacturers to position the asset for optimal pricing and reimbursement. When agreement cannot be reached on price or reimbursement terms, risk-sharing agreements allow broader access in exchange for the manufacturer bearing incrementally greater financial risk. Manufacturers have also built partnerships to uncover the real-world value of therapies and gain insight into usage and adherence patterns. Each market has its own challenges for promoting collaboration, requiring manufacturers to tailor their approach to the various national and local payers **CONCLUSION:** Early planning is imperative in value-focused health care. When early payer engagement succeeds, it provides manufacturers time to design informed strategies to meet payer valuation needs. Evidence development that is closely aligned with payer requirements results in therapies that are more cost effective and gain quicker market access, benefitting manufacturers, payers, and patients alike.

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EARLY NICE DECISION PROBLEM MEETINGS: IMPLICATIONS FOR CROSS-FUNCTIONAL INDUSTRY TEAMS

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The National Institute for Health and Care Excellence (NICE) in England and Wales is currently piloting a process whereby decision problem meetings are held several months before starting a technology appraisal, rather than approximately 10 weeks after formal invitation for the manufacturer to submit evidence, per current protocol. In general, the purpose and outcomes of the meeting, involving the NICE team and representatives from the evidence research group (ERG), do not change other than happening earlier. However, the meeting does allow manufacturers and sponsors to signal potential regulatory developments during the appraisal, ahead of the submission, to indicate potential inclusion and handling of patient access scheme proposals. For the meeting, an outline is required to demonstrate how the manufacturer/sponsor intends to approach the decision problem. This outline is to include, but is not limited to: evidence sources to be used; evidence likely to become available during the appraisal and how this might be managed; the planned approach to disease and economic modelling; potential challenges in interpreting the evidence; proposed approach to handling of uncertainty. If adopted, there are several implications of this new process for manufacturers/sponsors: market access strategy will need to be considered earlier than currently, with implications for data availability and analyses, value story development, positioning and indications, etc; cost-effectiveness models and their base cases will need earlier definition and completion; intentions regarding patient access schemes must be made before submission; ERGs may be reviewing limited published evidence in fast-moving therapy areas;, manufacturer market access groups will require more information from clinical, regulatory, medical affairs, modellers, epidemiologists much sooner that they currently do. Therefore, this seemingly simple change of meeting date relative to time of submission has important implications for manufacturers beyond their market access teams that require careful consideration in terms of planning and communication.

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THE IRISH COST-EFFECTIVENESS THRESHOLD: DOES IT SUPPORT RATIONAL RATIONING OR MIGHT IT LEAD TO SYSTEMATIC DAMAGE OF IRELAND'S HEALTH SYSTEM?

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Irish legislation recognises the need to consider the cost-effectiveness of health services, both for new interventions and their opportunity cost. Ireland did not have an explicit cost-effectiveness threshold until a 2012 agreement between the pharmaceutical industry and government established a €45,000/QALY threshold. It was agreed as part of a deal that provided cost savings on existing medications and only applies to pharmaceuticals: there is no official threshold for non-drug interventions. Drugs with cost-effectiveness ratios within the threshold are guaranteed reimbursement, whereas those exceeding the threshold may be approved following further negotiation. A number of drugs far exceeding the threshold have been reimbursed in Ireland in recent years. There are four reasons for concern regarding Ireland's threshold. Firstly, as a price floor not a ceiling it offers only a weak constraint on the introduction of cost-ineffective interventions, which leaves little scope for positive net health benefit. Secondly, that the threshold only applies to drugs creates potential for inconsistencies whereby relatively cost-effective non-drug interventions may not necessarily be approved, leading to sub-optimal resource allocation. Thirdly, the current threshold has no apparent empirical basis. Finally, recent efforts to determine the appropriate cost-effectiveness threshold in the UK have estimated a threshold of approximately £13,000/QALY. Assuming Ireland's threshold should be broadly comparable, the current Irish threshold is most probably too high. Consequently, reimbursing new interventions at and above the €45,000/QALY threshold is likely to result in net harm, as new drugs produce less health than the interventions they displace. The failure of Ireland's threshold to be empirically determined by the cost-effectiveness of services foregone means the requirements of current legislation are not being met and reimbursement decisions cannot be considered fully evidenced-based. It is likely the current threshold is excessive and will lead to systematic damage of the health system.

PHP285

AN ETHIC SYSTEM OVERVIEW: BRAZILIAN PERSPECTIVES FOR OBSERVATIONAL STUDIES

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BACKGROUND: Observational studies have been one of the hallmarks for the development of public health and health economics fields. It includes epidemiologic studies, evaluation of patterns of care, use of resources, cost of illness, analysis of safety and effectiveness of interventions from real world. However, there are different patterns of requirements for ethics reviews concerning observational studies, including vastly available models of ethics systems among different countries. Therefore, the objective of this study is to evaluate the ethics system, regulations and guidelines concerning observational studies in the selected countries. **METHODOLOGY:** Guidelines and regulations from Brazil, Argentina, Japan, New Zealand, Australia, USA and UK were reviewed to evaluate the ethics system and available guiding principle for observational studies. Additionally, a literature review was performed in the database Medline and SciELO mesh using the terms "ethics", "observational study" and "multicenter study" among other similar terms. **RESULTS:** In Brazil, same ethics regulation is applied for both interventional and observational projects, plus there is unsatisfactory ethics review timelines and duplicity of ethics review when considering multicenter studies. Specific pathways for multicenter studies are available only in New Zealand, Australia, USA and UK. For the exception of Brazil, other evaluated countries have specific guidelines, recommendations or regulations for observational studies. **CONCLUSIONS:** Brazil and Argentina still have a lot of